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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/863,976 | 05/23/2001 | Farzan Rastinejad | PC10228B | 1819 |

7590 11/28/2006

Paul H. Ginsburg
Pfizer Inc
20th Floor
235 East 42nd Street
New York, NY 10017-5755

| EXAMINER | |
|---|---|
| BETTON, TIMOTHY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/863,976 | RASTINEJAD ET AL. | |
| | Examiner | Art Unit | |
| | Timothy E. Betton | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29March2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *26-56* is/are pending in the application.

4a) Of the above claim(s) *56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 29, 2006 has been entered.

Claims 1-25 are cancelled. No new claims are added. Claims 26-56 are currently pending.

Applicants' arguments, filed 29 March 2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### *Information Disclosure Statement*

The IDS filed 14 December 2004. Sheet 1 of instant IDS is a duplication of sheet 1 of IDS filed 09 August 2004. Additionally, on same IDS filed 14 December 2004, the reference: Wuonola *et al.*, two references have been crossed-out on the IDS, however a copy of both abstracts are filed and recorded. The two references have been recorded and filed on an additional form 892.

### *Claim Rejection(s) – 35 USC§ 112, 1$^{ST}$ paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in MPEP 2164.01(a), " There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue."

*In re Wands* , set forth the following eight factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, 1ST paragraph:

1. The nature of the invention;
2. The state of the prior art;
3. The predictability or lack thereof in the art;
4. The amount of direction or guidance present;
5. The presence or absence of working examples;
6. The breadth of the claims;
7. The quantity of experimentation needed; and
8. The level of the skill in the art.

***The nature of the invention***

The invention is in the field of cancer treatment; therefore the nature of the invention is complex. Instant invention is drawn to methods of stabilizing mutant forms of tumor suppressor proteins of the p53 family in humans via interaction of organic non-peptide compounds.

***The state of the prior art and the predictability or lack thereof in the art***

The state of the art, pharmacology, involves screening *in vitro* and *in vivo* in order to determine which compounds exhibit pharmacological activities. There is no reasonable predictability even in view of the seemingly high level of skill in the art.

Through practicing of the instant invention, it is highly unlikely that the contemporary knowledge in the art would allow one of ordinary skill in the art to accept that the instantly claimed compounds or pharmaceutical compositions thereof are capable of detecting at the disclosed minimal concentration of 1 mM or less.

***The amount of direction or guidance present***

The amount of direction or guidance present in instant specification and claim set is deficient in light of the nature of the alleged invention (treatments for cancer). The disclosures of instant invention do not present sufficient direction or guidance within the disclosed steps of **contacting** and **measuring** at a concentration of 1 or less of the said compound.

***The presence or absence of working examples***

There is the presence of working examples, however the content of such examples are absent of specific details drawn to the embodiment of the invention of being able to elicit a therapeutic effective response by use of 1mM or less of said compound. In the instant specification (page 16, line 1-3), initial disclosure of 1 mM or less is disclosed as a preferred embodiment, yet there is no presence of a working example incorporating said range in reference to a criteria and/or model specifically elucidating reasonable success. Furthermore, in the instant specification (page 49,

line15-6), there is a specific disclosure of Compound X as being active at 0.03 mM in the assay of Example 3 (page 46). However, applicant has failed to satisfy a duty to disclose evidence supporting such a conclusion. The instant example 3 makes no prior mention of 0.03 mM in the actual process steps. There is no presence of specific data charting the use of said specified concentration (0.03 mM) reasonably connected to any criteria for success in the scope of invention of alleged claims.

In the instant specification (page 46, lines 9-11 and page 48, lines 3-5, respectively) discloses results of one embodiment of assaying, however there is **no** specific mention as to the exact concentration of Compound X used in the measuring step of the process. In another embodiment of assaying (page 48), it discloses that the p53 dependent activation of the reporter gene occurred within a relatively small concentration range as the effectiveness of the compounds at higher doses were limited by cell detachment. Again, however, there is no specific disclosure as to the exact concentration of said compound, which is directed toward the measuring step of the instant invention.

In instant claim 26 disclosed therein is the binding to one or more domains of said protein under physiological conditions and restoring or stabilizing a functional conformation therein. However, in the specification (page 48, lines 21-23) it discloses that a strong interaction with a small subset of the protein molecules that are in the transition state may function to block further deviation from the active conformation or facilitate reversion to the native conformation. A disclosure of native conformation is absent from the instant claims and provides no explanation elsewhere in relation to the

scope of invention. There are no working examples by which to distinguish one example of functional conformation in comparison to native conformation. Functional conformation is disclosed but it is unclear as to what is intended as the scope of invention. In the absence of functional conformation, what evidence is there that native conformation as disclosed would be enabling toward claimed invention.

Physiological conditions are not readily apparent from the working examples. Though in certain embodiments, living cells and transfected cells are disclosed, there are multiplicities of factors in relation to physiological conditions. There is an absence of proper explanation directed toward said working example. The **assay does not sufficiently emulate** tumor cells and/or p53 cells in normal homeostatic environment. Therefore, stabilization is a term relative to the disclosed working examples. In the specification (page 46), disclosure is made in reference to compounds that enhance the stability of the active conformation on newly synthesized p53 [to] allow the accumulation of steady state levels of functional p53 in a time-dependent manner. However, the disclosed working examples are absent of any detailed data to suggest reasonable stability, further raising enabling issues.

***The breadth of the claims, quantity of experimentation, and level of skill in the art***

The breadth of the claims is broad including variant factors, which would require continued exhaustive experimentation. The level of the skill in the art requires high expertise due to the nature of the invention (treatment of cancer).

Again, as stated in MPEP 2164.01(a), " There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue."

Subject claim 26 is not enabled due to a lack of sufficient evidence and experimentation that said compound of a concentration 1 mM or less could reasonably achieve what is allegedly disclosed as an effective treatment for cancer via method steps of contacting and measuring. Furthermore, in the instant specification (page 49, lines 17-24), applicants' disclose that nature of the compound interaction with p53 may not involve tight binding to the native protein structure. A strong interaction with a **small** subset of the protein molecules that are in the transition state may function to block further deviation from the active conformation or facilitate reversion to the native conformation. The above statement disclosed suggests the need for on-going experimentation. In conjunction with the lack of enablement for a compound with a concentration of 1mM or less in reference to alleged invention, the ability to bind effectively presents with fundamentally significant issues of enablement.

***Response to Remarks***

Applicants' remarks, filed 29 March 2006, have been fully considered but they are not deemed to be persuasive. Rejections not reiterated from previous office actions are hereby withdrawn. The above rejection is either reiterated or newly applied. They constitute the set presently being applied to the instant application.

***Conclusion***

Claims 26-55 stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

11/24/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER